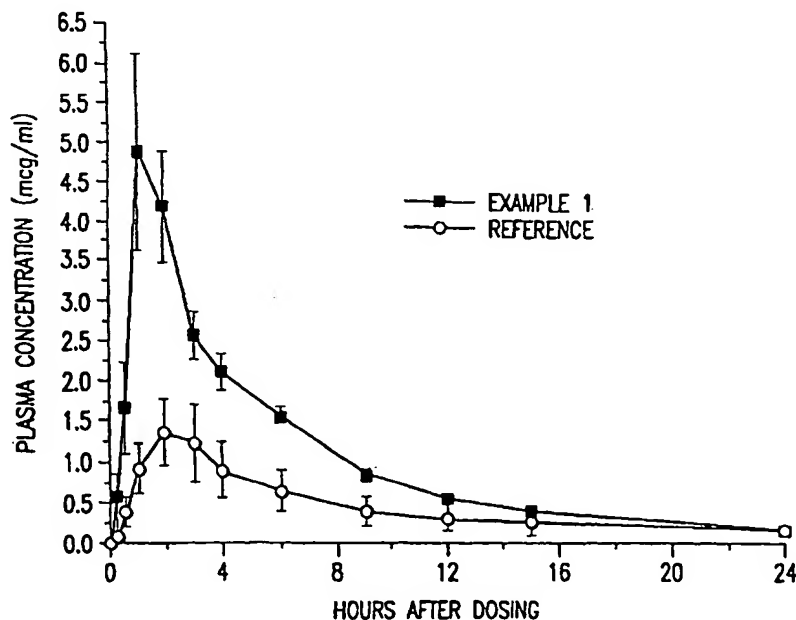




## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>7</sup> : A61K 47/44, A61P 3/06		A2	(11) International Publication Number: WO 00/57918
			(43) International Publication Date: 5 October 2000 (05.10.00)
(21) International Application Number: PCT/US00/07459		(81) Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: 21 March 2000 (21.03.00)			
(30) Priority Data: 09/283,356 31 March 1999 (31.03.99) US			
(71) Applicant: ABBOTT LABORATORIES [US/US]; D377/AP6D, 100 Abbott Park Road, Abbott Park, IL 60064-6050 (US).			
(72) Inventors: LIU, Rong (Ron); 973 Knowles Road, Gurnee, IL 60031 (US). PAN, Qinghai; 12589 West Meadow Circle, Lake Bluff, IL 60044 (US). HANSRANI, Pawan; 87 Chestnut Terrace, Buffalo Grove, IL 60089 (US).			
(74) Agents: SICKERT, Dugal, S. et al.; D377/AP6D, 100 Abbott Park Road, Abbott Park, IL 60064-6050 (US).		<p><b>Published</b></p> <p><i>Without international search report and to be republished upon receipt of that report.</i></p>	

(54) Title: NOVEL FORMULATIONS COMPRISING LIPID-REGULATING AGENTS



## (57) Abstract

The present invention is directed to a formulation comprising a lipid-regulating agent dissolved in a mixture of an oil and one or more surfactants to form a concentrate. This concentrate forms fine and stable emulsions upon gentle mixing with water or any aqueous solutions.

*FOR THE PURPOSES OF INFORMATION ONLY*

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

## Novel Formulations Comprising Lipid-Regulating Agents

Field of the Invention

5

The present invention relates to novel formulations comprising lipid-regulating agents.

10

Background of the Invention

15

2-[4-(4-chlorobenzoyl)phenoxy]-2-methyl-propanoic acid, 1-methylethylester, also known as fenofibrate, is representative of a broad class of compounds having pharmaceutical utility as lipid regulating agents. More specifically, this compound is part of a lipid-regulating agent class of compounds commonly known as fibrates, and is disclosed in U.S. Patent No. 4,058,552.

20

Fenofibrate has been prepared in several different formulations, c.f., U.S. Patent No. 4,800,079 and U.S. Patent No. 4,895,726. U.S. Patent No. 4,895,726 discloses a co-micronized formulation of fenofibrate and a solid surfactant.

25

U.S. Patent No. 4,961,890 discloses a process for preparing a controlled release formulation containing fenofibrate in an intermediate layer in the form of crystalline microparticles included within pores of an inert matrix. The formulation is prepared by a process involving the sequential steps of dampening said inert core with a solution based on said binder, then projecting said fenofibrate microparticles in a single layer onto said dampened core, and thereafter drying, before said solution based on said binder dissolves said fenofibrate microparticles, and repeating said three steps in sequence until said intermediate layer is formed.

35

European Patent Application No. EP0793958A2 discloses a process for producing a fenofibrate solid dosage form utilizing fenofibrate, a surface active agent and polyvinyl pyrrolidone in which the fenofibrate particles are mixed with a polyvinyl pyrrolidone solution. The thus obtained mixture is granulated with an aqueous solution of one or more surface active agents, and the granulate thus produced is dried.

PCT Publication No. WO 82/01649 discloses a fenofibrate formulation having granules that are comprised of a neutral core that is a mixture of saccharose and starch. The neutral core is covered with a first layer of fenofibrate, admixed with an excipient and with a second microporous outer layer of an edible polymer.

U.S. Patent No. 5,645,856 describes the use of a carrier for hydrophobic drugs, including fenofibrate, and pharmaceutical compositions based thereon. The carrier comprises a digestible oil and a pharmaceutically-acceptable surfactant component for dispersing the oil in vivo upon administration of the carrier, which comprises a hydrophilic surfactant, said surfactant component being such as not to substantially inhibit the in vivo lipolysis of the digestible oil.

Gemfibrozil is another member of the fibrate class of lipid-regulating agents. U.S. Patent No. 4,927,639 discloses a disintegratable formulation of gemfibrozil providing both immediate and sustained release, comprising a tablet compressed from a mixture of a first and second granulation, and a disintegration excipient operable to effect partial or complete disintegration in the stomach. The first granulation comprises finely divided particles of pure gemfibrozil granulated with at least one cellulose derivative, and the second granulation comprises finely

divided particles of pure gemfibrozil granulated with a pharmaceutically-acceptable water soluble or insoluble polymer which are then uniformly coated with a pharmaceutically-acceptable (meth)acrylate copolymer prior to admixture with the first granulation. The first and second granulations are present in the final composition in a ratio of from about 10:1 to about 1:10.

U.S. Patent 4,925,676 discloses a disintegratable gemfibrozil tablet providing both immediate and enteric release, which is compressed from a mixture of a first granulation of gemfibrozil with at least one acid-disintegratable binder, and a second granulation formed from the first granulation, but regranulated or coated with an alkali-disintegratable formulation of at least one substantially alkali-soluble and substantially acid-insoluble polymer.

Another class of lipid-regulating agents are commonly known as statins, of which pravastatin and atorvastatin are members. U.S. Patents 5,030,447 and 5,180,589 describe stable pharmaceutical compositions, which when dispersed in water have a pH of at least 9, and include a medicament which is sensitive to a low pH environment, such as prevastatin, one or more fillers such as lactose and/or microcrystalline cellulose, one or more binders, such as microcrystalline cellulose (dry binder) or polyvinylpyrrolidone (wet binder), one or more disintegrating agents such as croscarmellose sodium, one or more lubricants such as magnesium stearate and one or more basifying agents such as magnesium oxide.

It is an object of the present invention to provide formulations of lipid-regulating agents having enhanced bioavailability and longer half-life when compared to commercially available formulations.

### Summary of the Invention

5 The present invention is directed to a formulation comprising a lipid-regulating agent dissolved in a mixture of an oil and one or more surfactants to form a concentrate. This concentrate forms fine and stable emulsions upon gentle mixing with water or any aqueous solutions. The emulsions result in an increase in drug solubility and oral bioavailability.

10

The formulation may be administered directly, diluted into an appropriate vehicle for administration, encapsulated into soft or hard gelatin capsules for administration, or administered by other means obvious to those skilled in the art.

15

### Brief Description of the Drawings

20 Figure 1 is a graph showing the plasma concentration in fasted dogs of the formulation of Example 1 and a reference compound.

25

### Detailed Description of the Invention

The bulk lipid-regulating agent may be prepared by any available method, as for example the compound fenofibrate may be prepared by the procedure disclosed in U.S. Patent No. 4,058,552, or the procedure disclosed in U.S. Patent No. 4,739,101, both herein incorporated by reference.

30

The solution comprising the lipid-regulating agent is prepared by premixing the oil and one and more surfactants, then adding the lipid-regulating agent to the premix and mixing the resulting mixture well until dissolved.

35

The delivery system of the present invention results in increased solubility, half-life and bioavailability of the lipid-regulating agent. It can be further diluted with additional liquids or it may be thickened and/or stabilized with various pharmaceutical excipients to vary its existing properties.

Suitable oils include, but are not limited to, any pharmaceutically acceptable oil, such as, for example, Myvacet 9-08 (distillated acetylated monoglycerides: manufacturer), Myvacet 9-40 (distillated acetylated monoglycerides: manufacturer), Capmul PG-8 (propylene glycol and mono/di-caprylate; Abitec), Arlamol E (polyoxypropylene (15) stearyl alcohol; ICI), Captex 300 (glyceryl tricaprylate/caprate; Abitec), Labrafac Lipophile WL 1349 (triglyceride of caprylic/capric acid; Gattefosse), olive oil, Miglyol 812 ((caprylic/capric triglycerides; HULS America), sesame oil, Novol (oleyl alcohol; Croda). Preferred oils include Myvacet 9-08, Myvacet 9-40, and Capmul PG-8

Suitable surfactants include any surfactant in which fenofibrate is highly soluble. Such surfactants will typically be those with HLB values ranging from about 1 to about 20. Representative surfactants include Labrafac Lipophile WL 1349 (triglyceride of caprylic/capric acid; Gattefosse), Lauroglycol FCC (propylene glycol laurate; Gattefosse), Labrafil M 1944 CS (glyceryl and polyethylene glycol esters; Gattefosse), Span 80 (sorbitan monooleate; Sigma), Capmul MCM (mono/diglycerides of caprylic/capric acid in glycerol; Abitec), Arlacel 83 (sorbitan sesquioleate; ICI), Brij 93 (polyoxyethylene (2) oleyl ether; READ ICI), Acconon E (polyoxypropylene 15 stearyl ether; Abitec), Labrafil M 2125 CS (unsaturated polyglycolized glycerides; Gattefosse), Maisine 35-1 (glyceryl monolinoleate; Gattefosse), Sorbitan Oleate NF (Crill #4; Croda), Caprol 10G100 (decaglyceryl decaoleate;

Abitec), Labrafil Isostearique (triisostearin PEG 6 esters; Gattefosse), Caprol 3G0 triglyceryl monooleate; Abitec), Peceol (glyceryl monooleate; Gattefosse), G-950 (sorbitide dioleate; ICI), Arlacel 989 (polyoxyethylene castor wax; ICI), Labrafac CM 10 (polyglycolysed glycerides; Gattefosse), Labrafac CM 12 (polyglycolysed glycerides; Gattefosse), Labrasol (saturated C8-C10 polyglycolysed glycerides; Gattefosse), Tween 80 (polyoxyethylene (20) sorbitan monooleate; Sigma), Tween 85 (polyoxyethylene (20) sorbitan trioleate; Sigma), Pluronic L43 (copolymers of propylene oxide and ethylene oxide; BASF), Pluronic 17R4 (copolymers of propylene oxide and ethylene oxide; BASF), Cremophor EL (polyoxyl 35 castor oil; BASF), Accomid PK (palm kernelamide DEA; Abitec), Brij 30 (polyoxyethylene 4 lauryl ether; READ ICI), Arlasolve 200 liquid (polyoxyethylene (20) isohexadecyl ether; ICI), Arlacel 20 (sorbitan monolaurate; ICI), Renex 38 (alcohol ethoxylate; ICI), G-4280 (polyoxyethylene 80 sorbitan monolaurate; ICI), Caprol 6G20 (hexaglyceryl dioleate; Abitec), Crillet 4 Ultra (polysorbate 80; Croda), Crodesta SL-40 (sucrose laurate; Croda), Cirrasol G-265 (quaternary ammonium salt; ICI), Cirrasol G-1096 (polyoxyethylene sorbitol hexaoleate; ICI), Softigen 767 (caprylic/capric acid partial glyceride-6 EO; HULS America), Witconol 14 (polyglyceryl 4 oleate; Witco).

25

Preferred surfactants include Labrafac Lipophile WL 1349 (triglyceride of caprylic/capric acid; Gattefosse), Labrafac CM 10 and CM 12 (polyglycolysed glycerides; Gattefosse), Lauroglycol FCC (propylene glycol laurate; Gattefosse), Peceol (glyceryl monooleate; Gattefosse), Caprol 3G0 (triglyceryl monooleate; Abitec), Capmul MCM (mono/diglycerides of caprylic/capric acid in glycerol; Abitec), Labrasol (saturated C8-C10 polyglycolysed glycerides; Gattefosse), Tween 80 (polyoxyethylene (20) sorbitan monooleate; Sigma), Pluronic L43 (copolymers of propylene oxide; BASF), Pluronic 17R4 (copolymers of propylene oxide and ethylene oxide; BASF), Cremophor EL

35



(polyoxyl 35 castor oil; BASF), Brij 30 (polyoxyethylene 4 lauryl ether; READ ICI), Arlacel 20 (sorbitan monolaurate; ICI), Renex 38 (alcohol ethoxylate; ICI).

5           Other optional ingredients which may be included in the compositions of the present invention are those which are conventionally used in oil-based drug delivery systems, e.g. antioxidants such as, for example, tocopherol, ascorbyl palmitate, ascorbic acid, butylated hydroxytoluene,  
10           butylated hydroxyanisole, propyl gallate, etc.; pH stabilizers such as, for example, citric acid, tartaric acid, fumaric acid, acetic acid, glycine, arginine, lysine, potassium hydrogen phosphate, etc.; thickeners/suspending agents such as, for example, hydrogenated vegetable oils,  
15           beeswax, colloidal silicon dioxide, gums, celluloses, silicates, bentonite, etc.; flavoring agents such as, for example, cherry, lemon, aniseed flavors, etc.; sweeteners such as, for example, aspartame, saccharin, cyclamates, etc.; and co-solvents, such as, for example, ethanol,  
20           propylene glycol, polyethylene glycol, dimethyl isosorbide, etc.; adsorbents such as, for example, lactose, sorbitol, high molecular weight polyethylene glycols, such as, for example, PEG 1475, PEG 8000, etc.), and hydrophilic polymers, such as, for example, Avicel PH 101 (microcrystalline  
25           cellulose; FMC) hydroxypropylmethyl cellulose, etc.

          The resulting liquid comprising the lipid-regulating agent may be dosed directly for oral administration, diluted into an appropriate vehicle for oral administration, filled  
30           into soft or hard shells or capsules for oral administration, or delivered by some other means obvious to those skilled in the art. The said liquid can be used to improve the oral bioavailability and solubility of the said lipid-regulating agent.

35

          The invention will be understood more clearly from the following non-limiting representative examples:

Example 1

Myvacet 9-08 (40.2 gm) was mixed with propylene glycol  
5 laurate (13.4 gm). Fenofibrate (6.7 gm) was then added to  
the above mixture and mixed until completely dissolved. One  
drop of the solution was diluted with 10 ml of water and the  
droplet size was measured by laser light scattering as 2.95  
(m. 670 mg of the mixture (containing 67 mg of fenofibrate)  
10 was added to each soft gelatin capsule.

Example 2

Myvacet 9-08 (40.2 g) is mixed with propylene glycol  
15 laurate (13.4 g). Pravastatin (5.0 g) is then added to the  
above mixture and mixed until well dissolved. Appropriate  
amount of solution may be filled into capsules to provide  
the desired dose.

Example 3

The emulsion prepared by the process described in  
Example 1, and from a commercial fenofibrate composition,  
Lipanthyl 67M (Groupe Fournier) (Reference), were  
25 administered to a group of dogs at a dose of 67 mg  
fenofibrate/dog (10 mL emulsion or one capsule/dog). The  
plasma concentrations of fenofibric acid were determined by  
HPLC. Concentrations were normalized to a 6.7 mg/kg dose in  
each dog. Figure 1 presents the resulting data in graph  
30 form. The results provided as mean  $\pm$  SD, n=6, were as  
follows:

Lipanthyl 67M (Reference):

Cmax =  $1.88 \pm 0.97$  mcg/ml

35 Tmax =  $1.6 \pm 0.9$  hr

t<sub>1/2</sub> = 4.5 hr

AUC (0-24) =  $11.08 \pm 9.42$  mcg•hr/ml

Capsules of Example 1:

$C_{max} = 3.88 \pm 2.15$  mcg/ml

$T_{max} = 0.9 \pm 0.3$  hr

5  $t_{1/2} = 5.9$  hr

$AUC (0-24) = 17.37 \pm 10.58$  mcg•hr/ml

$C_{max}$  relative to Reference = 2.1

$AUC$  relative to Reference = 1.6

Claims

1. A composition comprising a lipid-regulating agent dissolved in at least one oil with one or more  
5 surfactants, wherein the mixture is capable of forming an emulsion upon dilution with an aqueous phase.
2. A composition of claim 1 wherein said lipid-regulating agent is a fibrate.
- 10 3. A composition of claim 2 wherein said fibrate is fenofibrate.
4. A composition of claim 1 wherein said lipid-regulating  
15 agent is a statin.
5. A composition of claim 4 wherein said statin is prevastatin.
- 20 6. A composition of claim 4 wherein said statin is atorvastatin.
7. A composition of claim 1 wherein at least one or more  
25 of said surfactants is triglyceride of caprylic/capric acid, propylene glycol laurate, glyceryl and polyethylene glycol esters, sorbitan monooleate, mono/diglycerides of caprylic/capric acid in glycerol, sorbitan sesquioleate, polyoxyethylene (2) oleyl ether, polyoxypropylene 15 stearyl ether, unsaturated  
30 polyglycolyzed glycerides, glyceryl monolinoleate, Crill #4, decaglyceryl decaoleate, triisostearin PEG 6 esters, triglyceryl monooleate, glyceryl monooleate, sorbide dioleate, polyoxyethylene castor wax, polyglycolysed glycerides, polyglycolysed glycerides,  
35 saturated C8-C10 polyglycolysed glycerides, polyoxyethylene (20) sorbitan monooleate, polyoxyethylene (20) sorbitan trioleate, copolymers of

- propylene oxide and ethylene oxide, copolymers of propylene oxide and ethylene oxide, polyoxyl 35 castor oil, palm kernelamide DEA, polyoxyethylene 4 lauryl ether, polyoxyethylene (20) isohexadecyl ether, sorbitan monolaurate, alcohol ethoxylate, polyoxyethylene 80 sorbitan monolaurate, hexaglyceryl dioleate, polysorbate 80, sucrose laurate, quaternary ammonium salt, polyoxyethylene sorbitol hexaoleate, caprylic/capric acid partial glyceride-6 EO, polyglyceryl 4 oleate.
8. A composition of claim 7 wherein at least one of said surfactants is selected from triglyceride of caprylic/capric acid, polyglycolysed glycerides, propylene glycol laurate, glyceryl monooleate, triglyceryl monooleate, mono/diglycerides of caprylic/capric acid in glycerol, saturated C8-C10 polyglycolysed glycerides, polyoxyethylene (20) sorbitan monooleate, copolymers of propylene oxide, copolymers of propylene oxide and ethylene oxide, polyoxyl 35 castor oil, polyoxyethylene 4 lauryl ether, sorbitan monolaurate, alcohol ethoxylate.
9. A composition of claim 1 wherein said oil is selected from distilled acetylated monoglycerides, distilled acetylated monoglycerides, propylene glycol and mono/di-caprylate, polyoxypropylene (15) stearyl alcohol, glyceryl tricaprylate/caprate, triglyceride of caprylic/capric acid, olive oil, caprylic/capric triglycerides, sesame oil, oleyl alcohol.
10. A composition of claim 9 wherein said oil is selected from distilled acetylated monoglycerides, distilled acetylated monoglycerides, and propylene glycol and mono/di-caprylate
11. A delivery system comprising a composition of claim 1.

12. A delivery system of claim 11 wherein said delivery system is an emulsion.
- 5 13. A delivery system of claim 11 wherein said delivery system is a capsule.
14. A method of treating hyperlipidemia comprising the administration of a composition of claim 1 to a  
10 patient.
15. A method of treating hyperlipidemia comprising the administration of a composition of claim 3 to a patient.
- 15 16. A method of treating hyperlipidemia comprising the administration of a composition of claim 11 to a patient.
- 20

1/1

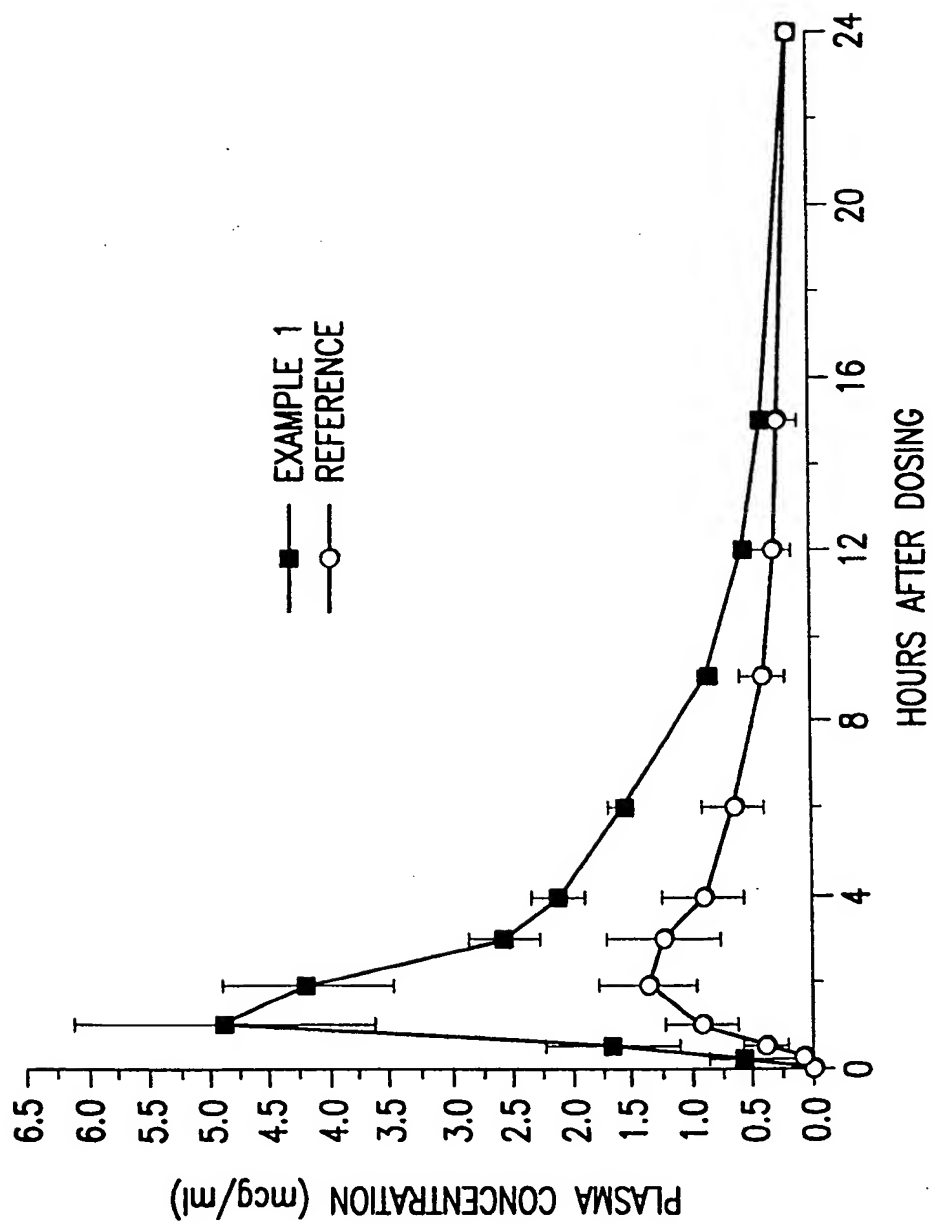


FIG.1

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
5 October 2000 (05.10.2000)

PCT

(10) International Publication Number  
**WO 00/57918 A3**

(51) International Patent Classification: **A61K 47/44**,  
A61P 3/06, A61K 31/19, 31/216, 31/22, 9/48

(21) International Application Number: PCT/US00/07459

(22) International Filing Date: 21 March 2000 (21.03.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
09/283,356 31 March 1999 (31.03.1999) US

(71) Applicant: **ABBOTT LABORATORIES** [US/US];  
D377/AP6D, 100 Abbott Park Road, Abbott Park, IL  
60064-6050 (US).

(72) Inventors: **LIU, Rong (Ron)**; 973 Knowles Road, Gurnee,  
IL 60031 (US). **PAN, Qinghai**; 12589 West Meadow Cir-  
cle, Lake Bluff, IL 60044 (US). **HANSRANI, Pawan**; 87  
Chestnut Terrace, Buffalo Grove, IL 60089 (US).

(74) Agents: **SICKERT, Dugal, S. et al.**; D377/AP6D, 100  
Abbott Park Road, Abbott Park, IL 60064-6050 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE,  
DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,  
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,  
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent  
(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent  
(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,  
MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,  
GA, GN, GW, ML, MR, NE, SN, TD, TG).

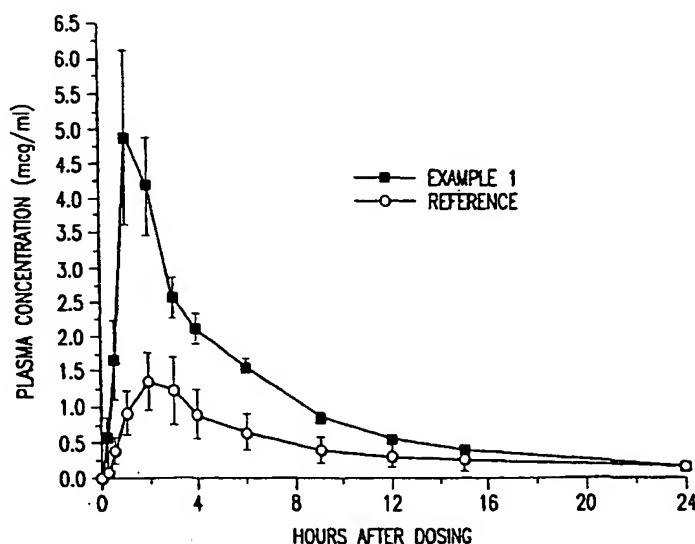
Published:

— With international search report.

(88) Date of publication of the international search report:  
18 January 2001

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: NOVEL FORMULATIONS COMPRISING LIPID-REGULATING AGENTS



(57) Abstract: The present invention is directed to a formulation comprising a lipid-regulating agent dissolved in a mixture of an oil and one or more surfactants to form a concentrate. This concentrate forms fine and stable emulsions upon gentle mixing with water or any aqueous solutions.



WO 00/57918 A3



# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/07459

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K47/44 A61P3/06 A61K31/19 A61K31/216 A61K31/22  
A61K9/48

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 24893 A (R.P.SCHERER LTD.,GB) 21 September 1995 (1995-09-21) cited in the application claims page 9, line 7 -page 11, line 11 page 14, line 1 -page 15, line 14 page 18, line 5 -page 19, line 1 page 25, line 3 - line 4 page 44, line 20 - line 25 ---	1-3,7,9, 11-16
X,P	WO 99 29300 A (RTP PHARMA INC.,CA) 17 June 1999 (1999-06-17) claims examples 1-11 page 6, line 11 -page 7, line 3 page 7, line 10 -page 8, line 17 page 9, line 4 - line 10 --- -/-	1-3,7,9, 11-16

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

9 October 2000

Date of mailing of the international search report

16/10/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Scarponi, U

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/07459

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 12528 A (SMB TECHNOLOGY, BE) 18 March 1999 (1999-03-18) claims example 1	1-16
A	EP 0 336 298 A (E.R.SQUIBB & SONS INC., U.S.A.) 11 October 1989 (1989-10-11) cited in the application claims	1, 4-6, 11-16

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/07459

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9524893 A	21-09-1995	AU 686767 B	12-02-1998
		AU 1897495 A	03-10-1995
		CA 2185347 A	21-09-1995
		EP 0750495 A	02-01-1997
		JP 10503750 T	07-04-1998
		US 5645856 A	08-07-1997
		US 6096338 A	01-08-2000
WO 9929300 A	17-06-1999	AU 1809499 A	28-06-1999
		AU 1817499 A	28-06-1999
		EP 1039893 A	04-10-2000
		NO 20002991 A	09-08-2000
		WO 9929316 A	17-06-1999
WO 9912528 A	18-03-1999	BE 1011363 A	03-08-1999
EP 336298 A	11-10-1989	US 5030447 A	09-07-1991
		AT 79030 T	15-08-1992
		AU 3027689 A	05-10-1989
		CA 1323836 A	02-11-1993
		CN 1036508 A, B	25-10-1989
		CY 1675 A	10-10-1993
		DE 68902344 D	10-09-1992
		DE 68902344 T	07-01-1993
		DK 155689 A	01-10-1989
		HK 40093 A	30-04-1993
		IE 62956 B	08-03-1995
		JP 2006406 A	10-01-1990
		JP 2935220 B	16-08-1999
		NZ 228076 A	26-04-1991
		SG 107292 G	24-12-1992
		US 5180589 A	19-01-1993
		ZA 8901424 A	25-10-1989

**THIS PAGE BLANK (USPTO)**